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The diagnosis of COPD in primary care; gender differences and the role of spirometry.

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Abstract

Background

Females with exacerbations of Chronic Obstructive Pulmonary Disease now account for one half of all hospital admissions for that condition and rates have been increasing over the last few decades. Differences in presentations of disease between genders have been shown in several conditions and this study explores whether there are inter gender biases in probable diagnoses in those suspected to have COPD.

Methods

445 individuals with a provisional diagnosis by their General Practitioner of “suspected COPD” or “definite COPD” were referred to a community Respiratory Assessment unit (CRAU) for tests including spirometry. Gender, demographics, respiratory symptoms and respiratory medical history were recorded. The provisional diagnoses were compared with the final diagnosis made after spirometry and respiratory specialist nurse review and the provisional diagnosis was either confirmed as correct or refuted as unlikely.

Results

Significantly more men (87.5%) had their diagnosis of “definite COPD” confirmed compared to 73.9% of women ($p=0.021$). When the GP suggested a provisional diagnosis of “suspected COPD” ($n=265$) at referral, this was confirmed in 60.9% of men and only 43.2% of women ($p=0.004$). There was a different symptom pattern between genders with women being more likely to report allergies, symptoms starting earlier in life, and being less likely than men to report breathlessness as the main symptom.

Conclusions

These results may suggest a difference between genders in some of the clinical features of COPD and a difference in likelihood of a GPs provisional diagnosis of COPD being correct. The study reiterates the absolute importance of spirometry in the diagnosis of COPD.

Background

Respiratory disease accounts for approximately 20% of all consultations in primary care, and is the second most common reason for admission to hospitals [1]. Much of the morbidity and mortality related to such diseases results from exacerbations. Frequent exacerbations of Chronic Obstructive Pulmonary Disease (COPD) are associated with more rapid decline in lung function [2]. Improving the identification of those with long term conditions such as COPD and ensuring effective management is crucial to minimise the burden of long term conditions. In the United Kingdom, this includes schemes such as the Quality Outcomes Framework (QOF) where general practices are rewarded for achieving targets in clinical indicators to improve diagnosis, build disease registers and provide interventions for those with long term conditions.

QOF points are given for confirmation of COPD with spirometry and annual reviews for those with COPD and asthma. This has ensured that more general practitioners are offering spirometry, but studies have shown that few nurses undertaking spirometry had undertaken training and few diagnosing COPD had specialist training [3, 4]

Current UK guidelines all highlight the importance of accurate diagnosis of COPD through a combination of history taking, examination, spirometry and specialist review where needed [5]. A Community Respiratory Assessment Unit (CRAU) was established in 2004 in West London to provide diagnostic support to primary care physicians working within the Hammersmith and Fulham area [6]. An audit of the first four years of the programme has been published [7] and patients were referred from over 20 different general practices. The main driver for referral was likely to be the QOF process and it is not possible to determine how representative those referred to CRAU are of others attending those practices.

In cardiac cases Mosca *et al* have shown that clinicians often fail to recognise cardiovascular risk in women [9]. Similarly in the field of lung disease Chapman *et al* [10] showed in 2001, using hypothetical scenarios, that COPD was given as the probable diagnosis significantly more often in men compared to women (58% vs 42%; $p < 0.05$). This study has not been updated to see if this trend still exists and has not been evaluated in a real population study. In recent years the worldwide prevalence of COPD has been growing faster for women compared to men in many countries such as the USA [11]. Admissions to hospital for

women with exacerbations of COPD have been steadily increasing and in the 2014 National COPD Audit in England and Wales women accounted for 51% of the admissions [8]. Infantino *et al* [12] suggest that women may not experience typical COPD symptoms. We have therefore explored which biases, if any, currently inform GP predicted diagnoses of COPD in men and women.

Methods

Gender, demographics, respiratory symptoms and history were examined for patients referred by a GP to a community Respiratory Assessment unit for diagnostic spirometry (CRAU) with a provisional diagnosis of “suspected COPD” or “definite COPD” over a 4 year period. The provisional diagnoses were compared with the final diagnosis after spirometry and respiratory specialist nurse review. Details of previous analyses from the CRAU database have been published elsewhere [6,7].

The CRAU consultation consisted of the following elements: obtaining a Respiratory history, measurement of Oxygen saturation, measurement of exhaled CO in smokers, spirometry +/- reversibility testing, checking of medications and inhaler technique, smoking cessation advice and advice regarding lifestyle changes (i.e nutrition, exercise). When, as a result of the consultation and investigations a specific diagnosis was explicit, appropriate self-management education was provided. Spirometry was carried out following a standard operational procedure based on key national and international guidance [3] using height, weight, ethnicity, gender and age. Usual exclusion criteria were used (e.g. unstable angina, haemoptysis, active tuberculosis or other respiratory infection, recent thoracic surgery) and three technically acceptable manoeuvres were required, (two within 100ml) to ensure reproducibility criteria, and diagnoses of COPD suggested according to GOLD criteria in place at the time[15]. Proformas were developed for GP referral, nurse consultation, and diagnostic reports to primary care. Referral forms required GPs to suggest a referral diagnosis by selecting one from a list which consisted of: suspected or confirmed asthma, suspected or confirmed COPD, unexplained breathlessness, and cough. Nurse history sheets identified current medications, past medical, family and smoking history as well as current

respiratory symptoms and their duration. Data from the GP referral, nursing history sheets, spirometry measurements and the GP report were entered in to SPSS for analysis.

The confirmed diagnosis, GP letter, spirometry results, and nursing history sheets were reviewed by a respiratory physician and compared to the original GP referral suspected diagnosis. On the basis of this data, a decision was made whether the GP referral diagnosis was accurate or incorrect.

Statistical analysis

All statistical analysis was carried out using the software program SPSS (Version 20.0). For all analyses, Pearson chi square tests and independent t tests were used to look at gender differences and differences between confirmed and refuted diagnoses. A statistical significance of $p < 0.05$ was used throughout.

Results

Between January 2005 and December 2008, 1,156 referrals were received by the Community Respiratory Assessment Unit. COPD was the single most prevalent referral indication and this report focuses on the 445 GP referrals for “suspected” or “definite COPD” (221 males, 224 females). These referrals were reviewed and a comparison made between GP referral diagnosis and final diagnosis from the unit for both males and females. Significant differences were found in the proportion of those with a confirmed “correct” referral diagnosis of COPD between men and women (men [72%] versus [56%] in women, $p=0.001$). When the GP suggested a provisional diagnosis of “definite COPD” ($n=180$) at referral, this was confirmed in 87.5% of men and 73.9% of women ($p=0.021$). When the GP suggested a provisional diagnosis of “suspected COPD” ($n=265$) at referral, this was confirmed in 60.9% of men and only 43.2% of women ($p=0.004$).

Patients with a suggested GP diagnosis of “definite COPD” ($n=180$)

The respiratory medical history taken from these patients showed that women with a referral diagnosis of definite COPD ($n=180$), irrespective of final outcome tended to be more likely to report a history of allergy symptoms compared to men (30.4% versus 17.0%; $p=0.099$). Although similarly not statistically significant women referred with definite COPD (not necessarily confirmed) were also less likely to report progressive breathlessness as their main symptom compared to men (women 58.7%, versus men 73.8%; $p=0.098$).

Gender differences in symptoms between males and females where provisional diagnosis of “definite COPD” was confirmed ($n=145$).

Of those with a *confirmed* CRAU diagnosis of COPD after a referral with definite COPD (Table 1), women were more likely to report symptoms of allergy than men (women 29%, versus men 19%; $p=0.001$). Women were also more likely to describe symptoms which were variable from day to day (women 25% versus men 12%; $p=0.050$).

Gender differences between symptoms in males and females where provisional diagnosis of “definite COPD” was refuted ($n=35$)

As part of the medical history individuals were asked if they had any allergies, and women who had a diagnosis of COPD refuted tended to report allergies more than men (women 33% versus men 0 % $p=0.067$). The majority of women in this group had no evidence of airways narrowing (75%). The other 6 individuals were classed as having restrictive spirometry (12.5%) or were thought to have asthma (12.5%). Of the 11 males 45.5% were on inhaled medication (excluding SABAs) at the time of referral, compared to 58% of women.

Patients with suggested GP diagnosis of “suspected COPD”(n=265)

There were significant differences in the number of women compared to men who had a diagnosis of COPD confirmed after the CRAU consultation (women , 43.2% versus men 60.9%, $p=0.004$). Females with suspected COPD were more likely to report allergies (women 32.6%, versus men 15%, $p=0.004$).

Gender differences in symptoms between males and females where provisional diagnosis of “suspected COPD” was confirmed (n=138)

Females with a confirmed diagnosis of COPD had a higher prevalence of allergies compared to men (female 40% versus men 13.5% $p=0.001$). They were also more likely to have had a family or personal history of atopic disease (women, 56% versus men 37% $p=0.019$) and were more likely to have symptoms starting later in life (5th,6th decade) (women 89.5% versus men 75%, $p=0.043$)

Gender differences in symptoms between males and females where provisional diagnosis of “suspected COPD” was refuted (n=127).

Women in this group had more symptoms of cough (women, 23% versus men 11.5%, $p=0.046$) and worse symptoms in the morning (women 28% versus men 25% $p=0.025$). Of those women with a refuted COPD diagnosis, 79% had spirometry results showing no airways narrowing, 13% had restrictive spirometry and 8% had a diagnosis of asthma. In this sub group, (women with a refuted diagnosis for suspected COPD), 79% were smokers or ex-smokers, compared to 91% of women with their suspected diagnosis confirmed. 27% of

males were on inhaled medication (excluding SABAs);, similar levels were evident in females, (28%).

A smaller number of men did not have the diagnosis of suspected COPD confirmed (39%) and these were likely to have either spirometry with no evidence of airways narrowing (69%), restrictive spirometry (15%), a non-respiratory cause (8%,) or asthma (6%). In this group 85% of men smoked compared to 95% of those with confirmed COPD.

Table 3 shows the likelihood of a GPs suspected or definite diagnosis of COPD being confirmed as correct, the results are much lower for those referred with suspected COPD (0.52) compared to those referred to with definite COPD (0.81). The results are also much lower for females (0.42 suspected COPD; 0.73 for definite COPD) than for men (0.61 suspected COPD; 0.88 for definite COPD).

Discussion

This study examined 445 referrals from general practice to a community respiratory assessment unit with either suspected or definite COPD. Amongst GP referrals with “suspected” and “definite” COPD, there were significant differences in final diagnosis between men and women after spirometry. In a review by Aryal *et al*, gender differences in the clinical presentation of COPD are discussed showing that women were more likely to report dyspnoea and more exacerbations compared to men [13]. In our study women were more likely to have a GP diagnosis of COPD amended after spirometry with no spirometric evidence of airway narrowing being found with the diagnosis being thought to be a non-respiratory condition. Amongst those referred with a suggested definite diagnosis of COPD this diagnosis was confirmed in 88% of men and 74% of women.

Where the GP diagnosis of COPD (either suspected or definite) was confirmed, there was a higher reported prevalence of allergies in the women’s respiratory medical histories, compared to the men. Women referred with definite COPD but in whom that diagnosis was refuted also had significantly higher prevalence of allergies when compared to men. One possible explanation for this could be the fact that these women actually had asthma, but with normal spirometry at the time of testing, but we have no follow up data on the eventual diagnosis of those in whom we were unable to confirm the GPs initial suspected diagnosis.

High levels of smoking were evident in both groups perhaps influencing GPs attitudes towards this diagnosis, as opposed to other possible diagnoses particularly in women. Infantino *et al* [10] suggest that women may not experience typical COPD symptoms. In the current study women appear to have a different symptom profile for COPD, and they were more likely to present with allergies and a family history of allergic disease, to present later in life than men, and less likely to present with breathlessness as the main symptom. An explanation for this is not immediately apparent but one possible hypothesis would be that more women than men in this study had the more recently described overlap syndrome,

where individuals, usually over the age of 40 present with symptoms of chronic airways disease with features of both asthma and COPD [14].

In line with current guideline recommendations a diagnosis of COPD was refuted if no evidence of airway narrowing was present. This of course depends upon the current classification of disease and occasionally patients with COPD present not with airway narrowing but with a productive cough and similarly some may present with breathlessness due to emphysema which can occur rarely with normal spirometry. Aberrant results may also occur if the patient is already on treatment at the time of referral for diagnostic assessment. A significant proportion of those with a refuted diagnosis of COPD were on inhaled medication and a proportion of these with no evidence of airways narrowing could instead have treated asthma. As the allergy signal seen amongst females in this dataset does not seem to be a strong differentiator of accurate diagnosis it is possible that the confirmed COPD group could contain those with asthma – COPD overlap syndrome (ACOS) or fixed airflow obstruction due to chronic asthma with or without smoking.

We cannot tell how representative the patients in this study are of those with COPD in general or how their history and symptom patterns are or are not typical of other patients in general practice. However this study suggests, as others have, that there are gender differences in the presentation and clinical profile of those with respiratory disease, but the clinical message is clear; the need for objective testing prior to the diagnosis of COPD is important for all but possibly even more so in females.

Conclusions

This study found significant differences between men and women in confirmed diagnoses of COPD after referral for suspected or definite COPD. Women were more likely to have a GP diagnosis of COPD which was amended after spirometry. High levels of smoking were evident in both groups perhaps influencing GPs towards this diagnosis, as opposed to other possible diagnoses particularly in women.

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Table 1 Results for correct /incorrect diagnosis for definite COPD

	Definite COPD n=180						
	Correct diagnosis (n=145)			Refuted diagnosis (n=35)			
	Males	Females	P value	Males	Females	P value	
N	77	68		11	24		
Age in years (SD)	67.4 (11.7)	70.7 (10.5)	0.067	63.7 (12.4)	70.0 (10.7)	0.134	
BMI (SD)	26.3 (5.8)	27.1 (9.7)	0.555	24.5 (4.7)	27.1 (5.8)	0.222	
RCP score* (SD)	3.9 (0.9)	3.9 (1.1)	0.119	3.7 (1.3)	3.6 (1.12)	1.000	
Pre-bronchodilator FEV ₁ FVC (SD)	48.5 (12.4)	52.9 (12.7)	0.064	72.4 (8.63)	69.5 (12.3)	0.512	
Past medical history							
Allergies, %	15 19.5	20 29.4	0.001	0 0.0	8 33.3	0.027	
Cough present, %	9 11.7	15 22.0	0.176	2 18.2	6 25	0.623	
Respiratory symptoms dating back to childhood, %	13 16.9	18 26.5	0.284	2 18.2	6 25	1.000	
Symptoms vary from day to day and time to time, %	9 11.7	17 25	0.050	3 27.3	6 25	0.852	
Symptoms worse in the morning, patient wakes prematurely, %	12 15.6	12 17.7	0.873	3 27.3	5 20.83	0.573	
Has a family or personal history of atopic disease including asthma, hayfever, and eczema, %	24 31.2	26 38.2	0.580	5 45.5	15 62.5	0.628	
Symptoms started in 5th, 6th or 7th decade, %	61 79.2	51 75	0.846	8 72.7	19 79.2	0.685	
Main symptom is progressive breathlessness on exertion over the last 1-3 years, %	56 72.7	39 57.4	0.175	9 81.8	15 62.5	0.526	
Patient is a smoker or ex-smoker, %	71 92.2	61 89.7	0.887	10 90.9	21 87.5	1.000	

* This is the score from the Royal College of Physicians 'three questions' used in asthma reviews [16]

Pearsons chi squared tests and independent t tests were used significance is P<0.05, Fischer's exact test reported when the cell count was below the expected number

Table 2 Results for correct/incorrect diagnosis for suspected COPD

	Suspected COPD n=265									
	Correct diagnosis (n=138)			Refuted diagnosis (n=127)						
	Males		Females		P value	Males		Females		P value
N	81		57			52		75		
Age in years (SD)	65.4	(11.2)	68.4	(10.3)	0.111	59.9	(11.9)	65.8	12.9)	0.009
BMI (SD)	26.5	(6.9)	25.9	(6.5)	0.692	26.9	(4.9)	27.9	(7.2)	0.379
RCP score* (SD)	4.1	(0.6)	3.9	(1.0)	0.315	3.7	(1.2)	3.8	(1.0)	0.573
Pre-bronchodilator FEV ₁ FVC (SD)	53.2	(11.2)	56.1	(9.2)	0.108	72.7	(13.1)	73.0	(8.5)	0.908
Past medical history										
Allergies, %	11	13.6	23	40.4	0.001	9	17.3	20	26.7	0.506
Cough present, %	20	24.7	8	14.0	0.280	6	11.5	17	22.7	0.046
Respiratory symptoms dating back to childhood, %	19	23.5	18	31.6	0.289	9	17.3	11	14.7	0.905
Symptoms vary from day to day and time to time, %	16	19.8	11	19.3	1.000	18	34.6	20	26.7	0.375
Symptoms worse in the morning, patient wakes prematurely, %	21	25.9	11	19.3	0.419	13	25.0	21	28.0	0.025
Has a family or personal history of atopic disease including asthma, hayfever, and eczema, %	30	37.0	32	56.1	0.019	19	36.5	32	42.7	0.707
Symptoms started in 5th, 6th or 7th decade, %	61	75.3	51	89.5	0.043	34	65.4	56	74.7	0.464
Main symptom is progressive breathlessness on exertion over the last 1-3 years, %	45	55.6	40	70.2	0.211	32	61.5	45	60.0	0.705
Patient is a smoker or ex-smoker, %	77	95.1	52	91.2	0.488	45	86.5	59	78.7	0.190

* This is the score from the Royal College of Physicians 'three questions' used in asthma reviews [16]

Pearsons chi squared tests and independent t tests were used significance is P<0.05, Fischer's exact test reported when the cell count was below the expected number

Table 3 The likelihood of a GPs suspected or definite diagnosis of COPD being confirmed as correct

	Overall (men and women)	Male	Female
<u>Suspected COPD (n=265)</u>	(138/265) = <u>0.52</u>	(81/133) = <u>0.61</u>	(57/132) = <u>0.43</u>
<u>Definite COPD (n=180)</u>	(145/180) = <u>0.81</u>	(77/ 88) = <u>0.88</u>	(68/ 92) = <u>0.74</u>